Decision Memo for Magnetic Resonance Angiography (MRA) (CAG-00142R)

Decision Summary

The Centers for Medicare & Medicaid Services (CMS) initiated this reconsideration to evaluate the current evidence for the non-covered indications for the Magnetic Resonance Angiography (MRA) National Coverage Determination (NCD) at section 220.3.C of the NCD Manual. CMS recently reconsidered the NCD for Magnetic Resonance Imaging (MRI) at section 220.2 and removed national non-coverage for MRI for blood flow determination, thereby permitting local Medicare contractors to make determinations within their respective jurisdictions. While reviewing published scientific evidence for that MRI reconsideration, CMS became aware of evidence that may speak to currently non-covered indications for MRA.

MRA is a specific application of MRI. CMS believes that the continued existence of separate NCDs is unnecessary, and that the provisions of the MRA NCD at section 220.3 should be merged under the NCD for MRI at section 220.2 Thus, section 220.3, MRA, of the NCD Manual, will no longer appear as a separate NCD.

The effect of this change will maintain existing national coverage at section 220.3.B by moving it into section 220.2.B. CMS will eliminate the non-coverage language in section 220.3.C, while moving it into section 220.2.D of the NCD Manual, and will permit local Medicare contractors to cover (or not cover) all indications of MRA (and MRI) that are not specifically nationally covered or nationally non-covered.

Back to Top

Decision Memo

TO: Administrative File: CAG # 00142R1 Magnetic Resonance Angiography

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SUBJECT: Final Decision Memorandum for CAG # 00142R1
Magnetic Resonance Angiography

June 3, 2010

DATE:

I. Final Decision

The Centers for Medicare & Medicaid Services (CMS) initiated this reconsideration to evaluate the current evidence for the non-covered indications for the Magnetic Resonance Angiography (MRA) National Coverage Determination (NCD) at section 220.3.C of the NCD Manual. CMS recently reconsidered the NCD for Magnetic Resonance Imaging (MRI) at section 220.2 and removed national non-coverage for MRI for blood flow determination, thereby permitting local Medicare contractors to make determinations within their respective jurisdictions. While reviewing published scientific evidence for that MRI reconsideration, CMS became aware of evidence that may speak to currently non-covered indications for MRA.

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The effect of this change will maintain existing national coverage at section 220.3.B by moving it into section 220.2.B. CMS will eliminate the non-coverage language in section 220.3.C, while moving it into section 220.2.D of the NCD Manual, and will permit local Medicare contractors to cover (or not cover) all indications of MRA (and MRI) that are not specifically nationally covered or nationally non-covered.

II. Background

Terminology

The prefix "angio" denotes relationship to a vessel, usually a blood vessel. (Dorland's Illustrated Medical Dictionary, 28th Ed.) The term may also apply to other types of vessels, e.g. lymphatic vessels or the bile duct. Angiography is the visualization (usually radiographic) of vessels (usually blood vessels). Visualization of other vessels is usually described with the appropriate additional prefix: lymphangiography for lymph vessels; cholangiography for the bile duct. Throughout this memorandum we use the term angiography and its various grammatical forms to refer to the imaging of blood vessels unless we specifically designate a different vessel type.

Magnetic resonance angiography (MRA) is a non-invasive diagnostic test that is an application of magnetic resonance imaging (MRI). By analyzing the amount of energy released from tissues exposed to a strong magnetic field, MRA provides images of normal and diseased blood vessels as well as visualization and quantification of blood flow through these vessels.

Phase contrast (PC) and time-of-flight (TOF) are the currently available MRA techniques. PC measures the difference between the phases of proton spins in tissue and blood, and measures both the venous and arterial blood flow at any point in the cardiac cycle. TOF measures the difference between the amount of magnetization of tissue and blood, and provides information on the structure of blood vessels, thus, indirectly measuring blood flow. Two-dimensional (2D) and three-dimensional (3D) images can be obtained using each method.

Contrast-enhanced MRA (CE-MRA) involves blood flow imaging after the patient receives an intravenous injection of a contrast agent. Gadolinium, a non-ionic element, is currently used as a magnetic resonance contrast agent. Gadolinium affects the way in which tissues respond to magnetization, resulting in better visualization of structures when compared to unenhanced studies. Unlike ionic (i.e., iodine-based) contrast agents used in contrast angiography (CA), allergic reactions to gadolinium are extremely rare. Additionally, gadolinium does not cause the kidney failure occasionally seen with ionic contrast agents. Physicians elect to use a specific MRA or CA technique based upon a patient's clinical situation.

III. History of Medicare Coverage

Section 220.3 of the NCD Manual speaks to coverage of MRA. CMS in October, 1995 set forth the original conditions under which MRA would be covered. Revisions to the policy took place in 1997, 1999, and 2003 to expand coverage for additional indications. Currently covered indications include using MRA for specific conditions to evaluate flow in internal carotid vessels of the head and neck, peripheral arteries of lower extremities, abdomen and pelvis and the chest. All other uses of MRA are nationally non-covered unless coverage is specifically indicated.

A. Current Request

CMS initiated this reconsideration to evaluate the current evidence for the non-covered indications for the Magnetic Resonance Angiography NCD at 220.3 of the National Coverage Determinations (NCD) Manual. CMS recently reconsidered the NCD for Magnetic Resonance Imaging (MRI) at 220.2 of the National Coverage Determinations Manual and removed national noncoverage for MRI for blood flow determination, thereby permitting local Medicare contractors to make determinations within their jurisdictions. While reviewing published scientific evidence for that MRI reconsideration we became aware of evidence that may speak to currently non-covered indications for MRA.

B. Benefit Category

Medicare is a defined benefit program. An item or service must fall within a benefit category as a prerequisite to Medicare coverage §1812 (Scope of Part A); §1832 (Scope of Part B) and §1861(s) (Definition of Medical and Other Health Services) of the Act. Magnetic resonance angiography is considered to be within the following benefit category: other diagnostic tests §1861(s) (3).

Medicare regulations at 42 CFR 410.32(a) state in part, that "…diagnostic tests must be ordered by the physician who is treating the beneficiary, that is, the physician who furnishes a consultation or treats a beneficiary for a specific medical problem and who uses the results in the management of the beneficiary's specific medical problem." Thus, except where other uses have been explicitly authorized by statute or CMS approves an additional preventive service under section 1861(ddd), Medicare does not cover diagnostic testing used for routine screening or surveillance.

IV. Timeline of Recent Activities

October 7, 2009	CMS opens this reconsideration of the NCD on Magnetic Resonance Angiography (MRA).
November 6, 2009	The initial 30 day public comment period ended. Three timely comments were received.
March 9, 2010	Proposed Decision Memorandum posted.
April 8, 2010	The second 30 day public comment period ended. Two comments were received.

V. FDA Status

The Food and Drug Administration (FDA) originally approved MRA imaging devices under a March 1988 pre-market approval (PMA) supplement for a 0.5 Tesla Picker MRI device with motion artifact suppression technology (MAST) software. These devices are approved for visualization of blood flow

VI. General Methodological Principles

When making national coverage determinations, CMS evaluates relevant clinical evidence to determine whether or not the evidence is of sufficient quality to support a finding that an item or service falling within a benefit category is reasonable and necessary for the diagnosis or treatment of illness or injury or to improve the functioning of a malformed body member. The critical appraisal of the evidence enables us to determine to what degree we are confident that: 1) the specific assessment question(s) can be answered conclusively; and 2) the intervention will improve health outcomes for beneficiaries. An improved health outcome is one of several considerations in determining whether an item or service is reasonable and necessary.

A detailed account of the methodological principles of study design that the Agency utilizes to assess the relevant literature on a therapeutic or diagnostic item or service for specific conditions can be found in Appendix A.

Public commenters sometimes cite the published clinical evidence and provide CMS with useful information. Public comments that provide information based on unpublished evidence, such as the results of individual practitioners or patients, are less rigorous and, therefore, less useful for making a coverage determination. CMS uses the initial comment period to inform the public of its proposed decision. CMS responds in detail to the public comments that were received in response to the proposed decision when it issues the final decision memorandum.

VII. Evidence

A. Introduction

Below is a summary of the evidence we considered during our review as well as additional evidence submitted through the public comment period.

The Medicare regulations at 42 CFR 410.32(a) state in part, that "…diagnostic tests must be ordered by the physician who is treating the beneficiary, that is, the physician who furnishes a consultation or treats a beneficiary for a specific medical problem and who uses the results in the management of the beneficiary's specific medical problem." Thus, we looked for evidence regarding how MRA might be used by the beneficiary's treating physician.

As the potential uses of MRA might involve a myriad of diseases in many organs, we focused on evidence regarding indications of which we became aware via public comment or our internal review.

B. Discussion of Evidence Reviewed

We did not review evidence for the indications that are currently covered nationally.

1. Questions

a. Does the evidence support a conclusion that MRA imaging guides physician management and thereby improves health outcomes in Medicare beneficiaries who have or are strongly suspected to have a dural arteriovenous fistula (DAVF)?

b. Does the evidence support a conclusion that MRA imaging guides physician management and thereby improves health outcomes in Medicare beneficiaries who are candidates for atrial fibrillation ablation?

Note: An arteriovenous fistula (AVF) is a vascular abnormality in which there is a direct connection of arterial and venous blood vessels without an intermediate capillary system. The dura mater is a membrane covering the central nervous system. Atrial fibrillation is an abnormal cardiac rhythm characterized by rapid, irregular heart beat.

2. External Technology Assessments

CMS did not request an external technology assessment (TA) on this issue.

3. Internal technology assessment

The reviewed evidence was gathered from a literature search of the PubMed database. CMS performed an extensive literature search utilizing PubMed for search terms involving MRA and 1) spinal and dural arteriovenous fistulae (DAVF) and 2) the pulmonary vein. Summaries are provided below.

DAVF

Leutmer et al. (2005)
Preangiographic evaluation of spinal dural arteriovenous fistulas with elliptic centric contrast-enhanced MR Angiography and effect on radiation dose and volume of iodinated contrast material.
Country: USA
Modality(ies): MRA, conventional angiography
Disease/Anatomy: Spinal dural AVF

Primary outcome measure(s): Correct prediction of Spinal dural AVF by MRA
Study type: Series
N=31

The authors proposed to test the hypothesis that MR angiography (MRA) can be used to detect spinal dural AVFs, predict the level of these fistulas, and reduce the radiation dose and volume of iodinated contrast material associated with conventional angiography. The authors examined 31 patients who presented with suspected spinal dural AVF between December 2000 and March 2004. All patients underwent MRA and conventional angiography. The effect of MRA on subsequent conventional angiography was assessed by analyzing total fluoroscopy time and volume of iodinated contrast material used.

At angiography, spinal dural AVFs were diagnosed in 22 of 31 patients, and MRA depicted an AVF in 20 of the 22 patients. MRA findings correctly predicted a negative angiogram in seven of nine cases. Of the 20 true-positive MRA results, the level of the fistula was included in the imaging volume in 14. In 13 of these 14 cases, MRA results correctly predicted the side and the level of the fistula to within one vertebral level. Fluoroscopy time and the volume of contrast agent were reduced by more than 50% in the 13 patients with a spinal dural AVF in whom MRA prospectively indicated the correct level. The authors concluded that contrast-enhanced MRA can be used to detect spinal dural AVFs, predict the level of fistulas, and substantially reduce the radiation dose and volume of contrast agent associated with catheter spinal angiography.

<u>Mull et al. (2007)</u>
Value and limitations of contrast-enhanced MR angiography in spinal arteriovenous malformations and dural arteriovenous fistulas.
Country: Germany
Modality(ies): MRA, DSA
Disease/Anatomy: Spinal AV abnormalities
Primary outcome measure(s): Detection of true spinal AV abnormalities by MRA
Study type: Consecutive series
N=34

The authors proposed to study the validity of MR angiography (MRA) for identification of spinal arteriovenous (AV) abnormalities. Thirty-four consecutive patients with suspicion of spinal vascular abnormalities underwent digital subtraction angiography (DSA) after MRA. The level and side of the suspected spinal dural arteriovenous fistula (SDAVF) and the feeding arteries in spinal arteriovenous malformations (SAVMs) were determined from the MRA and compared with DSA. DSA revealed SDAVF in 20 abnormalities of which 19 were spinal and 1 was tentorial with spinal drainage, as well as SAVMs in 11 patients. In 3 patients, MRA and DSA were both normal. For detection of spinal arteriovenous abnormalities, neither false-positive nor false-negative MRA results were obtained.

The MRA-derived level of the feeding artery in SDAVF agreed with DSA in 14 of 19 cases. In 5 cases, a mismatch of 1 vertebral level (not side) was noted for the feeding artery. For the tentorial AVF, only the spinal drainage was depicted; the feeding artery was outside the MRA field of view. In intradural SAVM, the main feeding artery was identified by MRA in 10 of 11 patients. MRA could differentiate between glomerular and fistulous SAVM in 4 of 6 cases and between sacral SDAVF and filum terminale SAVM in 2 of 5 cases. The authors concluded that MRA reliably detects or excludes various types of spinal AV abnormalities and localizes the (predominant) arterial feeder of most spinal AV shunts. Although classification of the subtype of SAVMs remains difficult, with MRA it greatly helps to focus subsequent DSA.

Saraf-Lavi et al. (2002)
Detection of spinal dural arteriovenous fistulae with MR imaging and contrast-enhanced MR angiography: sensitivity, specificity, and prediction of vertebral level. Country: USA
Modality(ies): MRI vs. (MRI + MRA)
Disease/Anatomy: 20 surgically proven dural AVF persons
Primary outcome measure(s):Sensitivity and specificity of reviewers to detect fistulae.
Study type: Convenience series
N=31, 20 diagnosed patients; 11 controls

The authors proposed to establish the sensitivity, specificity, and accuracy of MR imaging alone compared with MR imaging plus MRA in determining whether dural AVF are present and to establish the accuracy of MRA in predicting fistula level. Twenty patients with surgically proven dural AVF (diagnosed with radiographic digital subtraction angiography) and 11 control patients who had normal digital subtraction angiography findings underwent routine MR imaging plus 3D contrast-enhanced MRA of the spine. Images were reviewed in two stages (stage I, MR images only; stage II, MR images plus MR angiograms) by three neuroradiologists who were blinded to the final diagnoses.

The sensitivity, specificity, and accuracy of the three reviewers in detecting the presence of fistulae ranged from 85% to 90%, from 82% to 100%, and from 87% to 90%, respectively, for stage I, compared with values of 80% to 100%, 82%, and 81% to 94%, respectively, for stage II. For each reviewer, there was no significant difference between the values for stages I and II; however, among the reviewers, one of the more experienced neuroradiologists had significantly greater sensitivity than a less experienced neuroradiologist for stage II. On average, the percentage of true positive results for which the correct fistula level was predicted increased from 15% for stage I to 50% for stage II, and the correct level ± one level was predicted in 73% for stage II. MR evidence of increased intradural vascularity was significantly greater in patients with dural AVF. The authors concluded that the addition of MRA to standard MR imaging of the spine may improve sensitivity in the detection of spinal dural fistulae and that the principal benefit of MR angiography is in the improved localization of the vertebral level of the fistula, which potentially expedites the subsequent digital subtraction angiography study.

Meckel et al. (2007)
MR angiography of dural arteriovenous fistulas: diagnosis and follow-up after treatment using a time-resolved 3D contrast-enhanced technique.
Country: Switzerland
Modality(ies): MRA, DSA
Disease/Anatomy: dural arteriovenous fistula (DAVF).
Primary outcome measure(s): Accuracy of diagnosis
Study type: Retrospective review of series
N=14

The authors stated that Digital subtraction angiography (DSA) is the method of reference for imaging of dural arteriovenous fistula (DAVF). They aimed at retrospectively analyzing the value of different MR images including 3D contrast-enhanced MR angiography (MRA) with a high temporal resolution in diagnostic and follow-up imaging of DAVFs. Eighteen MR/MRA examinations from 14 consecutive patients (6 women, 8 men) with untreated (n=9) and/or treated (n=9) DAVFs were evaluated. All these patients underwent both MR and DSA in close succession for primary diagnosis of a DAVF or for follow-up evaluation of a treated DAVF. Two observers assessed all MR and MRA investigations for signs indicating the presence of a DAVF, for fistula characteristics such as fistula grading, location of fistulous point, and fistula obliteration after treatment. All results were compared with DSA findings.

On time-resolved 3D contrast-enhanced (TR 3D) MRA, the side and presence of all patent fistulas (n=13) were correctly indicated, and no false-positive findings were observed in occluded DAVFs (n=5). Grading of fistulas with this imaging technique was correct in 77% and 85% of patent fistulas for both readers, respectively. On T2-weighted images, signs indicative of a DAVF were encountered only in fistulas with cortical venous reflux (56%), whereas on 3D time-of-flight (TOF) MRA, most fistulas (88%) were correctly detected. In complete fistula occlusion, false-positive findings were encountered on both T2-weighted images and on TOF MRA images. The authors concluded that, in this study, TR 3D MRA proved reliable in detecting DAVFs and suitable for follow-up imaging, that the technique allowed within limitations to grade DAVFs, and finally, that although 3D TOF MRA can depict signs of DAVFs, its value for follow-up imaging is limited.

<u>Nijenhuis RJ et al. (2006)</u>
MR angiography of the great anterior radiculomedullary artery (Adamkiewicz artery) validated by digital subtraction angiography.
Country: Germany
Modality(ies): CE MRA with DSA as the comparator
Disease/Anatomy: Suspected spinal cord vascular pathology
Primary outcome measure(s): Agreement of DSA with MRA
Study type: Series
N=15

To validate the location and spatial configuration of the great anterior radiculomedullary artery, imaging of the anterior superficial spinal cord arteries by MR angiography via contrast-enhanced MR angiography (CE-MRA) was compared with digital subtraction angiography (DSA). Fifteen patients with suspected spinal cord vascular pathology underwent both spinal CE-MRA and selective spinal DSA. Two phase CE-MRA was performed with the use of a centric k-space filling scheme synchronized to the contrast bolus arrival. The level and side of the Adamkiewicz artery (AKA) origin were scored on the DSA and CE-MRA images and compared regarding image quality in terms of vessel conspicuity, contrast, continuity, sharpness, and background homogeneity on a relative 5-point scale.

Localization and spatial configuration of the AKA by CE-MRA was in agreement with DSA findings in 14 of 15 cases. One mismatch of 1 vertebral level (not side) appeared as a result of the tangled vascular pathology. Comparison of image quality revealed that DSA is superior to CE-MRA concerning vessel continuity, sharpness, and background homogeneity ($P < .001$). Overall vessel conspicuity and contrast were judged to be similar. The authors concluded that CE-MRA can visualize and localize the level of the AKA correctly and that image quality of CE-MRA is sufficient for detection of the AKA but is inferior to DSA.

Mascalchi et al. (2001)
Spinal vascular malformations: MR angiography after treatment.
Country: Italy
Modality(ies): 3D DCE MRA
Disease/Anatomy: Dural fistula
Primary outcome measure(s): Disappearance of enhancement in flow in perimedullary vessels and cord.
Study type: Series
N=34

The authors proposed to evaluate the role of magnetic resonance (MR) angiography in the assessment of spinal vascular malformation therapy. Thirty-four patients (10 women, 24 men) with spinal vascular malformations (30 dural arteriovenous fistulas, two perimedullary arteriovenous fistulas, and two intramedullary arteriovenous malformations) underwent MR angiography and MR imaging before and after endovascular or surgical treatment, over a period of 8 years. MR angiography showed residual flow in perimedullary vessels in seven patients with dural fistula after embolization with liquid adhesive. In all seven, treatment failure was confirmed with arteriography. Long-lasting disappearance of flow in perimedullary vessels was demonstrated at MR angiography in 22 patients with dural fistula. MR imaging demonstrated normalization of spinal cord volume in 16 of 22 patients and signal intensity on T2-weighted images in three patients. Disappearance of cord enhancement was observed in five of 21 patients and of perimedullary enhanced vessels in six of 13 patients. In one additional patient with dural fistula treated with embolization, early post-treatment MR angiography showed disappearance of flow in perimedullary vessels, which reappeared at follow-up and was consistent with reopening of a small residual fistula. Post-treatment MRA demonstrated transient reduction of flow in the nidus in two patients with intramedullary malformations treated with embolization. Permanent disappearance of flow in the perimedullary vessel was seen after endovascular treatment in two patients with perimedullary fistula. The authors concluded that MR angiography is more sensitive than MR imaging in depicting residual or recurrent flow in peri- or intramedullary vessels, which indicates patency of the vascular malformation.

Pulmonary Vein Imaging

We examined evidence regarding MRA for this indication in response to a public commenter.

Krishnam et al. (2009)
Three-dimensional imaging of pulmonary veins by a novel steady-state free-precession magnetic resonance angiography technique without the use of intravenous contrast agent: initial experience.
Country: USA
Modality(ies): MRA with and without contrast
Disease/Anatomy: Atrial fibrillation/ostial diameters
Primary outcome measure(s): Vascular definition artifacts, and ostial diameters
Study type: Consecutive series
N=40

In a study of 40 consecutive patients with a history of atrial fibrillation the authors aimed to compare the feasibility of 3-dimensional (3D) steady-state free-precession (SSFP) magnetic resonance angiography (MRA) using nonselective radiofrequency excitation for imaging of pulmonary veins (PVs) without intravenous gadolinium chelate and to correlate the results with conventional contrast-enhanced MRA (CE-MRA). Two readers assessed both datasets for vascular definition (from 0, not visualized, to 3, excellent definition), artifacts, and ostial diameters. Statistical analysis was performed using Wilcoxon, paired t test, and kappa coefficient. No significant difference was seen for visibility and sharpness of pulmonary venous segments between the datasets for each reader ($P > 0.05$). Reader 1 (2) identified 27 (28) and 35 (32) motion artifacts on SSFP and CE-MRA datasets, respectively. No significant difference was found to exist between ostial diameters on CE-MRA and SSFP datasets ($P > 0.05$). The authors concluded that 3D depiction of PVs without intravenous contrast is feasible with nonslice-selective SSFP MRA and that this (SSFP) MRA technique may be used in certain patients with atrial fibrillation to assess the number and size of PV ostia draining to the left atrium prior to radiofrequency ablation.

Allgayer et al. (2008)
Optimization of imaging before pulmonary vein isolation by radiofrequency ablation: breath-held ungated versus ECG/breath-gated MRA.
Country: Switzerland
Modality(ies): MRA, conventional angiography
Disease/Anatomy: Atrial fibrillation/left atrium, PVs, esophagus

Primary outcome measure(s): Anatomy assessment by MRA
Study type: Series
N=31

The authors begin by stating that isolation of the pulmonary veins has emerged as a new therapy for atrial fibrillation. They further state that pre-procedural magnetic resonance (MR) imaging enhances safety and efficacy and reduces radiation exposure of the patients and interventional team. They aimed at optimizing the MR protocol with respect to image quality and acquisition time. In 31 patients the anatomy of the pulmonary veins, left atrium and esophagus was assessed on a 1.5-Tesla scanner with four different sequences: (1) ungated two-dimensional true fast imaging with steady precession (2D-TrueFISP), (2) ECG/breath-gated 3D-TrueFISP, (3) ungated breath-held contrast-enhanced three-dimensional turbo fast low-angle shot (CE-3D-tFLASH), and (4) ECG/breath-gated CE-3D-TrueFISP. Image quality was scored from 1 (structure not visible) to 5 (excellent visibility), and the acquisition time was monitored. The pulmonary veins and left atrium were best visualized with CE-3D-tFLASH (scores 4.50 ± 0.52 and 4.59 ± 0.43) and ECG/breath-gated CE-3D-TrueFISP (4.47 ± 0.49 and 4.63 ± 0.39). Conspicuity of the esophagus was optimal with CE-3D-TrueFISP and 2D-TrueFISP (4.59 ± 0.35 and 4.19 ± 0.46) but poor with CE-3D-tFLASH (1.03 ± 0.13) ($p < 0.05$). Acquisition times were shorter for 2D-TrueFISP (44 ± 1 s) and CE-3D-tFLASH (345 ± 113 s) compared with ECG/breath-gated 3D-TrueFISP (634 ± 197 s) and ECG/breath-gated CE-3D-TrueFISP (636 ± 230 s) ($p < 0.05$). The authors concluded that an MR imaging protocol comprising CE-3D-tFLASH and 2D-TrueFISP allows assessment of the pulmonary veins, left atrium and esophagus in less than 7 min and they recommended it for pre-procedural imaging before electric isolation of pulmonary veins.

<u>Yu et al. (2008)</u>
Characteristics in image integration system guiding catheter ablation of atrial fibrillation with a common ostium of inferior pulmonary veins.
Country: China
Modality(ies): MRA or CT
Disease/Anatomy: Drug refractory Atrial fibrillation/LA, PVs
Primary outcome measure(s): : LA and PVs reconstruction by image integration to identify best treatment by ablation.
Study type: Consecutive series
N=1,226

A total of 1,226 patients with drug-refractory AF received magnetic resonance angiography (MRA) or multidetector computed tomography (MDCT) scan before ablation. Electrophysiological mapping was used to detect the focal triggers in paroxysmal AF. Basic catheter ablation strategy was circumferential PV isolation with "tricircle" under the guidance of the image integration system: two circles surround two superior PVs, and the other surrounds the common trunk. LA and PV reconstruction by image integration system showed a common pulmonary venous ostium of the right and left inferior PVs before ablation in 11 patients (0.9%). In six of the eleven the common ostium was an important triggering focus in paroxysmal AF. The authors concluded that a common ostium of the inferior PVs could be classified into two types according to the presence of a short common trunk or not and that a catheter ablation strategy of circumferential PV isolation employing "tricircle" technique under the guidance of an image integration system is a good choice.

Chang et al. (2007)
Morphological changes of the left atrial appendage after catheter ablation of atrial fibrillation.
Country: Taiwan
Modality(ies): MRA, conventional angiography
Disease/Anatomy: Atrial fibrillation/Left atrial appendage (LAA)
Primary outcome measure(s): LAA morphology before and after ablation was evaluated by three-dimensional MRA and used to potentially direct treatment.
Study type: RCT 40 paroxysmal AF, 15 controls no AF history
N=55

The authors state that though the left atrial appendage (LAA) has been proven to be the most important site of thrombus formation in patients with atrial fibrillation (AF) information regarding the morphometric alteration of the LAA related to the outcome of treatment of AF by ablation is lacking. Therefore they evaluated the long-term changes of the LAA morphology in patients undergoing catheter ablation of AF using magnetic resonance angiography (MRA). Using an RCT format Group 1 included 15 controls without any AF history. Group 2 included 40 patients with drug-refractory paroxysmal AF. This latter group was divided into two subgroups: group 2a included 30 patients without AF recurrence after pulmonary vein (PV) ablation. Group 2b included 10 patients with late recurrence of AF. The LAA morphology before and after (20 ± 11 months) ablation was evaluated by three-dimensional MRA.

The group 2 patients had a larger baseline LAA size (including the LAA orifice, neck, and length) and less eccentric LAA orifice and neck. After the AF ablation, there was a significant reduction in the LAA size in the group 2a patients, and the morphology of the LAA neck became more eccentric during the follow-up period. In group 2b, the LAA size increased and no significant change in the eccentricity of the orifice and neck was noted. The morphometric remodeling of the LAA in the AF patients could be reversed after a successful ablation of the AF. Progressive dilation of the LAA was noted in the patients with AF recurrence. The authors concluded that these structural changes in the LAA may play a role in reducing the potential risk of cerebrovascular accidents.

Toffanin et al. (2006)
Transoesophageal echocardiographic evaluation of pulmonary vein anatomy in patients undergoing ostial radiofrequency catheter ablation for atrial fibrillation: a comparison with magnetic resonance angiography.
Country: Italy
Modality(ies): MRA vs. Echo.
Disease/Anatomy: Atrial fibrillation
Primary outcome measure(s): Evaluation of PV anatomy in radiofrequency ablation for AF.
Study type: Consecutive series
N=45

The authors state that detailed definition of pulmonary vein (PV) anatomy is of great importance in patients undergoing radiofrequency catheter ablation for atrial fibrillation. The aim of their study was to assess the usefulness of transesophageal echocardiography (TOE) in defining the exact PV anatomy by comparing it with magnetic resonance angiography (MRA), which, they state, is proven to be very accurate. Forty-five consecutive patients affected by drug-refractory atrial fibrillation underwent radiofrequency catheter ablation. They were all studied with MRA and then with TOE in order to exclude intra-atrial thrombi and to assess PV anatomy.

TOE visualized the superior PVs in 100% of cases and the right and left inferior PVs in 98% and 94% of cases, respectively. Only 19 patients (42%) showed typical PV anatomy, with two left and two right distinct PV ostia. In 14 patients (31%), one or two intermediate right PVs and in 12 patients (27%) a common left trunk were detected. The concordance with MRA was high (95%). The authors concluded that TOE is accurate in assessing PV anatomy and in showing anatomic variations in the PV ostia compared with MRA.

Mansour et al. (2006)
Three-dimensional anatomy of the left atrium by magnetic resonance angiography: implications for catheter ablation for atrial fibrillation.
Country: USA
Modality(ies): MRA, conventional angiography
Disease/Anatomy: Atrial fibrillation/LA and PVs
Primary outcome measure(s): Pulmonary vein isolation (PVI) and catheter ablation success
Study type: Consecutive series
N=50

The authors state that during treatment by pulmonary vein isolation (PVI) for symptomatic drug refractory AF, delivery of ablation lesions to certain regions of the left atrium can be technically challenging. Among the most challenging regions are the ridges separating the left pulmonary veins (LPV) from the left atrial appendage (LAA), and the right middle pulmonary vein (RMPV) from the right superior (RSPV) and right inferior (RIPV) pulmonary veins. The authors aimed to provide a detailed anatomical characterization of these regions has not been previously reported. Magnetic resonance angiography (MRA) was performed in patients prior to undergoing PVI. Fifty consecutive patients with a RMPV identified by MRA were included in this study. Ridges associated with the left pulmonary veins were examined in an additional 30 patients who did not have a RMPV. Endoluminal views were reconstructed from the gadolinium-enhanced, breath-hold three-dimensional MRA data sets. Measurements were performed using electronic calipers.

The width of the ridge separating the LPV from the LAA was found to be 3.7 ± 1.1 mm at its narrowest point. The segment of this ridge with a width of 5 mm or less was 16.6 ± 6.4 mm long. The width of the ridges separating the RMPV from the RSPV and the RIPV was found to be 3.0 ± 1.5 mm and 3.1 ± 1.8 mm, respectively. There were no significant differences between LPV ridges for patients with versus without a RMPV. The authors concluded that the width of the ridges of atrial tissue separating LPV from the LAA and the RMPV from its neighboring veins may explain the technical challenge in obtaining stable catheter positions in these areas and that a detailed assessment of the anatomy of these regions may improve the safety and efficacy of catheter ablation at these sites.

Anselme et al. (2006)
MR evaluation of pulmonary vein diameter reduction after radiofrequency catheter ablation of atrial fibrillation. Country: France

Modality(ies): MRA, conventional angiography
Disease/Anatomy: Drug refractory atrial fibrillation
Primary outcome measure(s): Pre and post ablation MRA evaluation success.
Study type: Consecutive series
N=50

Fifty consecutive patients aged 52 ± 12 years suffering from drug refractory atrial fibrillation (AF) underwent baseline and post-ablation MR angiography (MRA) at a mean follow-up of 4 ± 3.5 months. Pulmonary vein (PV) disconnection was performed with a maximum energy delivery of 30 W. MRA allowed a two-plane measurement of each PV ostium. After ablation, no significant stenosis was observed, and only 1/194 (0.5%) and 3/194 (2%) PVs had a diameter reduction of 31-40% in the coronal and axial planes, respectively. There was a significant overall post-procedural PV narrowing of 4.9% in the coronal plane and 6.5% in the axial plane (P=ns between both planes). Using a maximal power delivery limited to 30W, no significant PV stenosis was observed at mid-term follow-up. The authors concluded that MRA is an efficient technique that can be used in pre- and postoperative evaluation of AF patients and that late PV anatomical assessment is needed to confirm their results.

Mlcochova et al. (2005)
Magnetic resonance angiography of pulmonary veins: implications for catheter ablation of atrial fibrillation.
Country: Czech Republic
Modality(ies): 3D MRA
Disease/Anatomy: Atrial fibrillation/PV ostia
Primary outcome measure(s): Ostia anatomy
Study type: Series
N=40

Because catheter ablation of atrial fibrillation (AF) requires exact anatomical information about pulmonary venous (PV) ostia, the authors evaluated the anatomy of pulmonary veins (PVs) using three-dimensional (3D) reconstructions of magnetic resonance angiography (MRA). Contrast-enhanced MRA of the PVs was performed in 40 patients) with paroxysmal (30 patients) or persistent (10 patients) AF, scheduled for circumferential ablation around PV ostia. PV ostial anatomy and diameters were evaluated from multiplanar reconstructions and compared with 3D reconstructions. Thirty (75%) patients presented with a common left-sided antrum (21 short and 9 long trunk), while additional PVs were found on right side in 23%. PV ostia were oblong in shape (mean diameters 17.0 ± 4.3 vs 10.5 ± 2.5 mm by two-dimensional (2D) measurements, and 20.8 ± 7.6 mm vs 12.9 ± 3.3 mm by 3D reconstruction, in long and short axis, respectively). There was a correlation between measurements obtained from 2D and 3D images, although 3D imaging provided slightly larger diameters. The authors concluded that MRA with 3D reconstructions is an important technique for preprocedural assessment of PVs that allows full understanding of their anatomy and size and that this information may be important for selection of appropriate tools.

Jayam et al. (2005)
Atrial volume reduction following catheter ablation of atrial fibrillation and relation to reduction in pulmonary vein size: an evaluation using magnetic resonance angiography
Country: USA (JHU)
Modality(ies): CE-MRA
Disease/Anatomy: Atrial fibrillation
Primary outcome measure(s): MRA comparison of LA volume before and after ablation.
Study type: Series
N=51

The purpose of this study was to evaluate the impact of segmental isolation of PVs on the volume of the left atrium and its relation to the decrease in the size of the pulmonary veins. Gadolinium enhanced Magnetic Resonance Angiography (MRA) was performed in 51 AF patients before and 6 approximately 8 weeks post PV isolation, using cooled radio-frequency (RF) energy. Three-dimensional reconstruction with maximum intensity projections and multiplanar reformations was performed. Oblique coronal projections were used to measure the ostial size of PVs. Three orthogonal dimensions of LA chamber were measured and computed to assess the volume of the left atrium. The mean LA volume decreased by 15.7% after ablation ($p<0.001$). The mean PV ostial diameter decreased by 11%, from 18.3 ± 0.8 mm to 16.7 ± 1.0 mm ($p=0.005$). Moderate PV stenosis was noted in two veins out of the 192 veins analyzed. There was a significant correlation between changes in the size of PV ostium to that of the LA. The authors concluded that catheter ablation of AF using a segmental PV isolation approach results in a significant reverse remodeling in the left atrium and that significant stenosis of the PVs appears to be rare after the segmental isolation procedure.

Cirillo et al. (2005)
Magnetic Resonance angiography of the pulmonary veins before and after radiofrequency ablation for atrial fibrillation.
Country: Italy
Modality(ies): MRA, conventional angiography
Disease/Anatomy: Atrial fibrillation/PV-atrio junction
Primary outcome measure(s): MRA
Study type: Series
N=50 MRA before ablation, 18 of them after

In order to study the usefulness of magnetic resonance angiography (MRA) in imaging of the pulmonary veins (PV) before and after radiofrequency ablation procedures in patients with atrial fibrillation 50 patients with atrial fibrillation underwent MRA prior to ablation and 18 patients also underwent post-procedure MRA. Images were acquired with 3D-spoiled gradient echo sequences after intravenous administration of the paramagnetic contrast medium gadopentetate dimeglumine; an automatic triggering device was used to start the angiographic sequence. Postprocessing was performed with maximum intensity projection (MIP) and virtual endoscopy (VE) software.

The venoatrial junction was visualized with MRA VE in 49 of 50 patients (98.0%). Twenty-seven patients out of 49 (55.1%) had two PV ostia on both sides, 13 (26.5%) had two right ostia and a single common left ostium, 5 (10.2%) had supernumerary PV and 4 (8.2%) had both a supernumerary right PV and a single common left ostium. Flythrough navigation showed the number and spatial arrangement of second-order PV branches in 48 out of 49 patients (98.0%). In postablation examinations, mild stenosis was detected with MIP and VE in 17 out of 83 PV examined (20.5%). The authors concluded that their study confirmed the clinical value of MRA for visualizing PV ostia in patients undergoing radiofrequency ablation for atrial fibrillation. The state that before the ablation procedure, MRA allows an accurate evaluation of PV number, shape and size and that after the procedure, MRA is useful in screening for post-ablation stenosis and describing the location and severity of stenosis when present.

Hauser et al. (2004)

A method for the determination of proximal pulmonary vein size using contrast-enhanced magnetic resonance angiography
Country: USA (Harvard)
Modality(ies): CE-MRA
Disease/Anatomy: Atrial fibrillation
Primary outcome measure(s): Proximal PV size
Study type: Consecutive series
N=24

The authors aimed to develop a reproducible method for characterizing the anatomy of the proximal pulmonary veins. They state that contrast-enhanced three-dimensional magnetic resonance angiography (CE-MRA) is a commonly requested test before and after radiofrequency ablation for the treatment of atrial fibrillation but that, while CE-MRA readily visualizes the pulmonary veins, there is no standardized method for determining their size and cross-sectional anatomy. They utilized 24 consecutive patients referred for pulmonary vein CE-MRA before an elective ablation procedure for the treatment of atrial fibrillation and analyzed their data. Detailed measurements of the pulmonary vein diameter, circumference, and cross-sectional area were obtained at three locations: the juncture of the pulmonary vein with the left atrium (LA) (position 1J), the narrowest segment within 5 mm of the juncture (position 2(5mm)), and at the location in the sagittal plane at which the pulmonary veins separate from the LA and from each other (position 3Sag). Intraobserver and interobserver variabilities were also determined for each method.

The left lower pulmonary vein was significantly smaller than the other pulmonary veins at positions 1J and 2(5mm) ($p < 0.05$). The right upper pulmonary vein was significantly larger than the other pulmonary vein at position 3Sag ($p < 0.05$). At positions 1J and 2(5mm), the diameter had a low correlation with the circumference and cross-sectional area. At position 3Sag, the major and minor axis dimensions had a very high correlation with the circumference and cross-sectional area. The intraobserver and interobserver variabilities were substantially lower (better) for position 3Sag. The authors concluded that pulmonary vein diameter measurements are highly variable and do not reflect true anatomic variation in cross-sectional anatomy and noted that a sagittal method of determining pulmonary vein size was highly reproducible and may therefore be advantageous for use in patients likely to need serial examinations.

4. MEDCAC

A Medicare Evidence Development Coverage Advisory Committee (MEDCAC) meeting was not convened on this issue.

5. Evidence-based guidelines

We did not find evidence-based guidelines relevant to this decision.

6. Professional Society Position Statements

We received a position statement in the form of a combined comment from The American College of Cardiology (ACC), American College of Radiology (ACR), American Society of Neuroradiology (ASNR), North American Society for Cardiovascular Imaging (NASCI), and the Society for Cardiovascular Magnetic Resonance (SCMR). They were in favor of combining the currently separate NCDs, allowing local Medicare contractor discretion to cover use of MRA for additional indications which are currently non-covered, and they recommended national coverage for MRA of the pulmonary veins before and after radiofrequency ablation for atrial fibrillation. (See comments from "second comment period" below)

7. Expert Opinion

We did not receive any expert opinions on the proposed decision during the comment period.

8. Public Comments

Public comment sometimes cites the published clinical evidence and gives CMS useful information. The CMS uses the initial public comments to inform its proposed decision. The CMS responds in detail to the public comments on a proposed decision when issuing the final decision memorandum.

Initial Comment Period: October 7, 2009 through November 6, 2009

During this public comment period, CMS received a total of three timely comments. Comments were received from a cardiologist, the American Health Insurance Plans (AHIP), and a marketer/manufacturer of a contrast agent indicated for the use of MRA. Of the three comments, one recommended the addition of pulmonary vein evaluation pre atrial fibrillation ablation to the list of covered indications but did not submit evidence to support the recommendation. One commenter provided literature citations and/or other materials with comments but no new scientific publications were uncovered. Full text comments without personal health information can be viewed at: http://www.cms.gov/mcd/viewpubliccomments.asp?nca_id=231.

Second Comment Period: March 9, 2010 through April 8, 2010

During the second comment period, two timely comments were received. One commenter was in favor of merging the MRA and MRI NCDs while the other was opposed. The commenter in favor also supports full national coverage for MRA of the pulmonary veins before and after radiofrequency ablation for atrial fibrillation. The other commenter suggested three additional indications of MRA they believe should be nationally covered. Both commenters support local Medicare contractor discretion for additional indications which are currently non-covered. The comments and CMS' responses are summarized below:

Comment in support of the proposed decision to merge the provisions of the MRA NCD at 220.3 of the Medicare NCD Manual under the NCD for MRI at 220.2 of the NCD Manual:

Comment

The commenter agrees that MRA is a type of MRI and the provisions of MRA should be merged under the MRI NCD.

Response

CMS appreciates the supportive comments.

Comment opposed to the proposed decision to merge the provisions of the MRA NCD at 220.3 of the Medicare NCD Manual under the NCD for MRI at 220.2 of the NCD Manual:

Comment

While the commenter suggested that MRA is the general term encompassing all of MR imaging, the commenter believes the existence of separate NCDs on MRI and MRA is necessary. The commenter believes that MRI and MRA are two important yet vastly different applications of MR and therefore require separate NCDs, noting that MRI is generally accepted as an evaluation of soft tissue and MRA is an evaluation of vascularity.

Response

CMS appreciates the comment yet we believe that MR encompasses both MRI and MRA. We are concerned that the coexistence of separate NCDs related to the use of MR to image blood flow and blood vessels may result in uncertainty about which NCD is determining coverage for a specific indication. We believe that the administratively appropriate action to resolve this overall issue as well as the evidentiary questions contained in this final decision is to merge the provisions of the MRA NCD into the MRI NCD.

Comments in support of the proposed decision to permit local Medicare contractors to cover (or not cover) all indications of MRA that are not specifically nationally covered or nationally non-covered:

Comment

Both commenters support local Medicare contractors to cover the use of MRA for indications which are currently non-covered. This flexibility will allow the local contractors to make the most appropriate determinations based on results obtained from diagnostic tests performed, data in the medical literature, and information obtained from treating physicians.

Response

CMS appreciates the supportive comments.

Comment

One commenter supports full coverage for MRA of the pulmonary veins before and after radiofrequency ablation for atrial fibrillation, believing the evidence reviewed in the proposed decision memorandum demonstrates that those patients who are candidates show a clear benefit from the use of contrast-enhanced MRA.

Response

CMS appreciates the comment, yet based on the current evidence, we cannot confidently determine that these diagnostic tests are reasonable and necessary for all beneficiaries nationally, for MRA of the pulmonary veins before and after radiofrequency ablation for atrial fibrillation, and who are suspected of having these conditions. Overall, the body of evidence suggests that treating physicians can use MRA assessment to manage the care of patients who are known or strongly suspected to have DAVF and that physicians can use MRA assessment to manage the care of beneficiaries who are candidates for ablation therapy for chronic atrial fibrillation. Although the reviewed studies' conclusions may be generalizable to the core Medicare beneficiary population, these supporting clinical studies are largely comprised of small case series, which have limited methodologic rigor and correspondingly limited evidentiary weight.

Comment

One commenter recommended that "MR perfusion imaging in acute stroke, utilization of MR perfusion imaging in brain tumors, and the use of MRA to evaluate polycystic disease patients to determine if their renal blood flow is decreasing as this is often a sign of disease progression," be nationally covered.

Response

CMS appreciates the comment but believes that the current NCDs for MRI and MRA already address these three areas of care in the "Head and Neck" and "Imaging the Renal Arteries and the Aortoiliac Arteries in the Absence of AAA or Aortic Dissection" sections. Any question of coverage beyond the nationally determined indications would now be left to local Medicare contractor discretion.

VIII. CMS Analysis

National coverage determinations (NCDs) are determinations by the Secretary with respect to whether or not a particular item or service is covered nationally by Medicare (§1869(f)(1)(B) of the Act). In order to be covered by Medicare, an item or service must fall within one or more benefit categories contained within Part A or Part B, and must not be otherwise excluded from coverage. Moreover, with limited exceptions the items or services must be "reasonable and necessary for the diagnosis or treatment of illness or injury or to improve the functioning of a malformed body member." See §1862(a)(1)(A) of the Act. This section presents the agency’s evaluation of the evidence considered and conclusions reached for the assessment

The Medicare regulations at 42 CFR 410.32(a) state in part, that "…diagnostic tests must be ordered by the physician who is treating the beneficiary, that is, the physician who furnishes a consultation or treats a beneficiary for a specific medical problem and who uses the results in the management of the beneficiary's specific medical problem."

We considered the evidence in the hierarchical framework of Fryback and Thornbury (1991) where Level 2 addresses diagnostic accuracy, sensitivity, and specificity of the test; Level 3 focuses on whether the information produces change in the physician's diagnostic thinking; Level 4 concerns the effect on the patient management plan and Level 5 measures the effect of the diagnostic information on patient outcomes. Most studies have focused on test characteristics and changes in physician diagnostic thinking and have not considered health outcomes, such as mortality or morbidity. We believe that health outcomes are more important than test characteristics.

Questions

a. Does the evidence support a conclusion that MRA imaging guides physician management in Medicare beneficiaries who have or are strongly suspected to have a dural arteriovenous fistula (DAVF)?

b. Does the evidence support a conclusion that MRA imaging guides physician management in Medicare beneficiaries who are candidates for atrial fibrillation ablation?

CMS reviewed the limited evidence on the use of MRA in evaluation, treatment planning and results re: spinal/dural AVFs. Responding to public comment, we also investigated the use of MRA for guiding physician management of beneficiaries who are candidates for ablation for atrial fibrillation. In a number of studies the reports of MRA utilization alone and in comparison to other modalities were found to be useful.

Overall, the body of evidence suggests that treating physicians can use MRA assessment to manage the care of patients who are known or strongly suspected to have DAVF and that physicians can use MRA assessment to manage the care of beneficiaries who are candidates for ablation therapy for chronic atrial fibrillation. We note that many of the reviewed studies included significant numbers of older subjects that their conclusions may be generalizable to the core Medicare beneficiary population. However, these supporting clinical studies are largely comprised of small case series, which have limited methodologic rigor and correspondingly limited evidentiary weight. Thus, based on the current evidence, we cannot confidently determine that these diagnostic tests are reasonable and necessary for all beneficiaries nationally who are suspected of having these conditions.

Magnetic resonance angiography has been widely available for many years and we are unaware of specific safety concerns beyond those of angiography and magnetic resonance imaging themselves. The natural evolution of medical information since the 2003 publication of the original MRA NCD has not shown any significant reason to continue to maintain two separate NCDs on this indication of magnetic resonance imaging.

For any individual beneficiary the usefulness of MRA to guide the treating physician's management of the beneficiary's condition may be affected by the beneficiary's specific medical problem, the availability of results of other diagnostic tests and the expertise of the interpreting physician. We believe in this case that our local administrative contractors, who may more readily obtain this information, can make these determinations within their jurisdictions. We do not believe that a national coverage determination is the most appropriate way to address this topic at this time.

As we noted earlier in this document, we believe that the coexistence of separate NCDs on MRI for blood flow at 220.2 and MRA at 220.3 is no longer necessary. We are concerned that the situation may result in uncertainty about which NCD determines coverage for the specified indication. We believe that the appropriate administrative action to resolve this overall issue as well as the evidentiary questions contained in this final decision is to merge the provisions of the Magnetic Resonance Angiography NCD at 220.3 of the NCD Manual into the NCD for Magnetic Resonance Imaging (MRI) at 220.2 of the National Coverage Determinations Manual.

The effect of this change would maintain existing national coverage at 220.3.B by moving it into 220.2. Local Medicare contractors will have discretion to cover (or not cover) all indications of MRA that are not nationally covered or nationally non-covered.

XI. Conclusion

The Centers for Medicare & Medicaid Services (CMS) initiated this reconsideration to evaluate the current evidence for the non-covered indications for the Magnetic Resonance Angiography (MRA) National Coverage Determination (NCD) at section 220.3.C of the NCD Manual. CMS recently reconsidered the NCD for Magnetic Resonance Imaging (MRI) at section 220.2 and removed national non-coverage for MRI for blood flow determination, thereby permitting local Medicare contractors to make determinations within their respective jurisdictions. While reviewing published scientific evidence for that MRI reconsideration, CMS became aware of evidence that may speak to currently non-covered indications for MRA.

MRA is a specific application of MRI. CMS believes that the continued existence of separate NCDs is unnecessary, and that the provisions of the MRA NCD at section 220.3 should be merged under the NCD for MRI at section 220.2 Thus, section 220.3, MRA, of the NCD Manual, will no longer appear as a separate NCD.

The effect of this change will maintain existing national coverage at section 220.3.B by moving it into section 220.2.B. CMS will eliminate the non-coverage language in section 220.3.C, while moving it into section 220.2.D of the NCD Manual, and will permit local Medicare contractors to cover (or not cover) all indications of MRA (and MRI) that are not specifically nationally covered or nationally non-covered

APPENDIX A

General Methodological Principles of Study Design

(Section VI of the Decision Memorandum)

When making national coverage determinations, CMS evaluates relevant clinical evidence to determine whether or not the evidence is of sufficient quality to support a finding that an item or service is reasonable and necessary. The overall objective for the critical appraisal of the evidence is to determine to what degree we are confident that: 1) the specific assessment questions can be answered conclusively; and 2) the intervention will improve health outcomes for patients.

We divide the assessment of clinical evidence into three stages: 1) the quality of the individual studies; 2) the generalizability of findings from individual studies to the Medicare population; and 3) overarching conclusions that can be drawn from the body of the evidence on the direction and magnitude of the intervention's potential risks and benefits.

The methodological principles described below represent a broad discussion of the issues we consider when reviewing clinical evidence. However, it should be noted that each coverage determination has its unique methodological aspects.

Assessing Individual Studies

Methodologists have developed criteria to determine weaknesses and strengths of clinical research. Strength of evidence generally refers to: 1) the scientific validity underlying study findings regarding causal relationships between health care interventions and health outcomes; and 2) the reduction of bias. In general, some of the methodological attributes associated with stronger evidence include those listed below:

- Use of randomization (allocation of patients to either intervention or control group) in order to minimize bias.

- Use of contemporaneous control groups (rather than historical controls) in order to ensure comparability between the intervention and control groups.
- Prospective (rather than retrospective) studies to ensure a more thorough and systematical assessment of factors related to outcomes.
- Larger sample sizes in studies to demonstrate both statistically significant as well as clinically significant outcomes that can be extrapolated to the Medicare population. Sample size should be large enough to make chance an unlikely explanation for what was found.
- Masking (blinding) to ensure patients and investigators do not know to which group patients were assigned (intervention or control). This is important especially in subjective outcomes, such as pain or quality of life, where enthusiasm and psychological factors may lead to an improved perceived outcome by either the patient or assessor.

Regardless of whether the design of a study is a randomized controlled trial, a non-randomized controlled trial, a cohort study or a case-control study, the primary criterion for methodological strength or quality is the extent to which differences between intervention and control groups can be attributed to the intervention studied. This is known as internal validity. Various types of bias can undermine internal validity. These include:

- Different characteristics between patients participating and those theoretically eligible for study but not participating (selection bias).
- Co-interventions or provision of care apart from the intervention under evaluation (performance bias).
- Differential assessment of outcome (detection bias).
- Occurrence and reporting of patients who do not complete the study (attrition bias).

In principle, rankings of research design have been based on the ability of each study design category to minimize these biases. A randomized controlled trial minimizes systematic bias (in theory) by selecting a sample of participants from a particular population and allocating them randomly to the intervention and control groups. Thus, in general, randomized controlled studies have been typically assigned the greatest strength, followed by non-randomized clinical trials and controlled observational studies. The design, conduct and analysis of trials are important factors as well. For example, a well designed and conducted observational study with a large sample size may provide stronger evidence than a poorly designed and conducted randomized controlled trial with a small sample size. The following is a representative list of study designs (some of which have alternative names) ranked from most to least methodologically rigorous in their potential ability to minimize systematic bias:

Randomized controlled trials

Non-randomized controlled trials
Prospective cohort studies
Retrospective case control studies
Cross-sectional studies
Surveillance studies (e.g., using registries or surveys)
Consecutive case series
Single case reports

When there are merely associations but not causal relationships between a study's variables and outcomes, it is important not to draw causal inferences. Confounding refers to independent variables that systematically vary with the causal variable. This distorts measurement of the outcome of interest because its effect size is mixed with the effects of other extraneous factors. For observational, and in some cases randomized controlled trials, the method in which confounding factors are handled (either through stratification or appropriate statistical modeling) are of particular concern. For example, in order to interpret and generalize conclusions to our population of Medicare patients, it may be necessary for studies to match or stratify their intervention and control groups by patient age or co-morbidities.

Methodological strength is, therefore, a multidimensional concept that relates to the design, implementation and analysis of a clinical study. In addition, thorough documentation of the conduct of the research, particularly study selection criteria, rate of attrition and process for data collection, is essential for CMS to adequately assess and consider the evidence.

Generalizability of Clinical Evidence to the Medicare Population

The applicability of the results of a study to other populations, settings, treatment regimens and outcomes assessed is known as external validity. Even well-designed and well-conducted trials may not supply the evidence needed if the results of a study are not applicable to the Medicare population. Evidence that provides accurate information about a population or setting not well represented in the Medicare program would be considered but would suffer from limited generalizability.

The extent to which the results of a trial are applicable to other circumstances is often a matter of judgment that depends on specific study characteristics, primarily the patient population studied (age, sex, severity of disease and presence of co-morbidities) and the care setting (primary to tertiary level of care, as well as the experience and specialization of the care provider). Additional relevant variables are treatment regimens (dosage, timing and route of administration), co-interventions or concomitant therapies, and type of outcome and length of follow-up.

The level of care and the experience of the providers in the study are other crucial elements in assessing a study's external validity. Trial participants in an academic medical center may receive more or different attention than is typically available in non-tertiary settings. For example, an investigator's lengthy and detailed explanations of the potential benefits of the intervention and/or the use of new equipment provided to the academic center by the study sponsor may raise doubts about the applicability of study findings to community practice.

Given the evidence available in the research literature, some degree of generalization about an intervention's potential benefits and harms is invariably required in making coverage determinations for the Medicare population. Conditions that assist us in making reasonable generalizations are biologic plausibility, similarities between the populations studied and Medicare patients (age, sex, ethnicity and clinical presentation) and similarities of the intervention studied to those that would be routinely available in community practice.

A study's selected outcomes are an important consideration in generalizing available clinical evidence to Medicare coverage determinations. One of the goals of our determination process is to assess health outcomes. These outcomes include resultant risks and benefits such as increased or decreased morbidity and mortality. In order to make this determination, it is often necessary to evaluate whether the strength of the evidence is adequate to draw conclusions about the direction and magnitude of each individual outcome relevant to the intervention under study. In addition, it is important that an intervention's benefits are clinically significant and durable, rather than marginal or short-lived. Generally, an intervention is not reasonable and necessary if its risks outweigh its benefits.

If key health outcomes have not been studied or the direction of clinical effect is inconclusive, we may also evaluate the strength and adequacy of indirect evidence linking intermediate or surrogate outcomes to our outcomes of interest.

Assessing the Relative Magnitude of Risks and Benefits

Generally, an intervention is not reasonable and necessary if its risks outweigh its benefits. Health outcomes are one of several considerations in determining whether an item or service is reasonable and necessary. CMS places greater emphasis on health outcomes actually experienced by patients, such as quality of life, functional status, duration of disability, morbidity and mortality, and less emphasis on outcomes that patients do not directly experience, such as intermediate outcomes, surrogate outcomes, and laboratory or radiographic responses. The direction, magnitude, and consistency of the risks and benefits across studies are also important considerations. Based on the analysis of the strength of the evidence, CMS assesses the relative magnitude of an intervention or technology's benefits and risk of harm to Medicare beneficiaries.

APPENDIX B Pub. 100-03 Medicare National Coverage Determinations Manual

220.2 - Magnetic Resonance Imaging (MRI) (Various Effective Dates Below)
A. General

1. Method of Operation

Magnetic Resonance Imaging (MRI), formerly called nuclear magnetic resonance (NMR), is a non-invasive method of graphically representing the distribution of water and other hydrogen-rich molecules in the human body. In contrast to conventional radiographs or computed tomography (CT) scans, in which the image is produced by X-ray beam attenuation by an object, MRI is capable of producing images by several techniques. In fact, various combinations of MRI image production methods may be employed to emphasize particular characteristics of the tissue or body part being examined. The basic elements by which MRI produces an image are the density of hydrogen nuclei in the object being examined, their motion, and the relaxation times, and the period of time required for the nuclei to return to their original states in the main, static magnetic field after being subjected to a brief additional magnetic field. These relaxation times reflect the physical-chemical properties of tissue and the molecular environment of its hydrogen nuclei. Only hydrogen atoms are present in human tissues in sufficient concentration for current use in clinical MRI.

Magnetic Resonance Angiography (MRA) is a non-invasive diagnostic test that is an application of MRI. By analyzing the amount of energy released from tissues exposed to a strong magnetic field, MRA provides images of normal and diseased blood vessels, as well as visualization and quantification of blood flow through these vessels.

2. General Clinical Utility

Overall, MRI is a useful diagnostic imaging modality that is capable of demonstrating a wide variety of soft-tissue lesions with contrast resolution equal or superior to CT scanning in various parts of the body.

Among the advantages of MRI are the absence of ionizing radiation and the ability to achieve high levels of tissue contrast resolution without injected iodinated radiological contrast agents. Recent advances in technology have resulted in development and Food and Drug Administration (FDA) approval of new paramagnetic contrast agents for MRI which allow even better visualization in some instances. Multislice imaging and the ability to image in multiple planes, especially sagittal and coronal, have provided flexibility not easily available with other modalities. Because cortical (outer layer) bone and metallic prostheses do not cause distortion of MR images, it has been possible to visualize certain lesions and body regions with greater certainty than has been possible with CT. The use of MRI on certain soft tissue structures for the purpose of detecting disruptive, neoplastic, degenerative, or inflammatory lesions has now become established in medical practice.

Phase contrast (PC) and time-of-flight (TOF) are some of the available MRA techniques at the time these instructions are being issued. PC measures the difference between the phases of proton spins in tissue and blood and measures both the venous and arterial blood flow at any point in the cardiac cycle. TOF measures the difference between the amount of magnetization of tissue and blood and provides information on the structure of blood vessels, thus indirectly indicating blood flow. Two-dimensional (2D) and three-dimensional (3D) images can be obtained using each method.

Contrast-enhanced MRA (CE-MRA) involves blood flow imaging after the patient receives an intravenous injection of a contrast agent. Gadolinium, a non-ionic element, is the foundation of all contrast agents currently in use. Gadolinium affects the way in which tissues respond to magnetization, resulting in better visualization of structures when compared to un-enhanced studies. Unlike ionic (i.e. iodine-based) contrast agents used in conventional contrast angiography (CA), allergic reactions to gadolinium are extremely rare. Additionally, gadolinium does not cause the kidney failure occasionally seen with ionic contrast agents. Digital subtraction angiography (DSA) is a computer-augmented form of CA that obtains digital blood flow images as contrast agent courses through a blood vessel. The computer "subtracts" bone and other tissue from the image, thereby improving visualization of blood vessels. Physicians elect to use a specific MRA or CA technique based upon clinical information from each patient.

B. Nationally Covered MRI and MRA Indications

1. MRI

Although several uses of MRI are still considered investigational and some uses are clearly contraindicated (see subsection C), MRI is considered medically efficacious for a number of uses. Use the following descriptions as general guidelines or examples of what may be considered covered rather than as a restrictive list of specific covered indications. Coverage is limited to MRI units that have received FDA premarket approval, and such units must be operated within the parameters specified by the approval. In addition, the services must be reasonable and necessary for the diagnosis or treatment of the specific patient involved.

a. Effective November 22, 1985, MRI is useful in examining the head, central nervous system, and spine. Multiple sclerosis can be diagnosed with MRI and the contents of the posterior fossa are visible. The inherent tissue contrast resolution of MRI makes it an appropriate standard diagnostic modality for general neuroradiology.

b. Effective November 22, 1985, MRI can assist in the differential diagnosis of mediastinal and retroperitoneal masses, including abnormalities of the large vessels such as aneurysms and dissection. When a clinical need exists to visualize the parenchyma of solid organs to detect anatomic disruption or neoplasia, this can be accomplished in the liver, urogenital system, adrenals, and pelvic organs without the use of radiological contrast materials. When MRI is considered reasonable and necessary, the use of paramagnetic contrast materials may be covered as part of the study. MRI may also be used to detect and stage pelvic and retroperitoneal neoplasms and to evaluate disorders of cancellous bone and soft tissues. It may also be used in the detection of pericardial thickening. Primary and secondary bone neoplasm and aseptic necrosis can be detected at an early stage and monitored with MRI. Patients with metallic prostheses, especially of the hip, can be imaged in order to detect the early stages of infection of the bone to which the prosthesis is attached.

c. Effective March 22, 1994, MRI may also be covered to diagnose disc disease without regard to whether radiological imaging has been tried first to diagnose the problem.

d. Effective March 4, 1991, MRI with gating devices and surface coils, and gating devices that eliminate distorted images caused by cardiac and respiratory movement cycles are now considered state of the art techniques and may be covered. Surface and other specialty coils may also be covered, as they are used routinely for high resolution imaging where small limited regions of the body are studied. They produce high signal-to-noise ratios resulting in images of enhanced anatomic detail.

2.MRA (MRI for Blood flow)

Currently covered indications include using MRA for specific conditions to evaluate flow in internal carotid vessels of the head and neck, peripheral arteries of lower extremities, abdomen and pelvis, and the chest. Coverage is limited to MRA units that have received FDA premarket approval, and such units must be operated within the parameters specified by the approval. In addition, the services must be reasonable and necessary for the diagnosis or treatment of the specific patient involved.

a. Head and Neck

Effective April 15, 2003, studies have proven that MRA is effective for evaluating flow in internal carotid vessels of the head and neck. However, not all potential applications of MRA have been shown to be reasonable and necessary. All of the following criteria must apply in order for Medicare to provide coverage for MRA of the head and neck:

- MRA is used to evaluate the carotid arteries, the circle of Willis, the anterior, middle or posterior cerebral arteries, the vertebral or basilar arteries or the venous sinuses;
- MRA is performed on patients with conditions of the head and neck for which surgery is anticipated and may be found to be appropriate based on the MRA. These conditions include, but are not limited to, tumor, aneurysms, vascular malformations, vascular occlusion or thrombosis. Within this broad category of disorders, medical necessity is the underlying determinant of the need for an MRA in specific diseases. The medical records should clearly justify and demonstrate the existence of medical necessity; and,
- MRA and CA are not expected to be performed on the same patient for diagnostic purposes prior to the application of anticipated therapy. Only one of these tests will be covered routinely unless the physician can demonstrate the medical need to perform both tests.

b. Peripheral Arteries of Lower Extremities

Effective April 15, 2003, studies have proven that MRA of peripheral arteries is useful in determining the presence and extent of peripheral vascular disease in lower extremities. This procedure is non-invasive and has been shown to find occult vessels in some patients for which those vessels were not apparent when CA was performed. Medicare will cover either MRA or CA to evaluate peripheral arteries of the lower extremities. However, both MRA and CA may be useful in some cases, such as:

- A patient has had CA and this test was unable to identify a viable run-off vessel for bypass. When exploratory surgery is not believed to be a reasonable medical course of action for this patient, MRA may be performed to identify the viable runoff vessel; or,
- A patient has had MRA, but the results are inconclusive.

c. Abdomen and Pelvis

i. Pre-operative Evaluation of Patients Undergoing Elective Abdominal Aortic Aneurysm (AAA) Repair

Effective July 1, 1999, MRA is covered for pre-operative evaluation of patients undergoing elective AAA repair if the scientific evidence reveals MRA is considered comparable to CA in determining the extent of AAA, as well as in evaluating aortoiliac occlusion disease and renal artery pathology that may be necessary in the surgical planning of AAA repair. These studies also reveal that MRA could provide a net benefit to the patient. If preoperative CA is avoided, then patients are not exposed to the risks associated with invasive procedures, contrast media, end-organ damage, or arterial injury.

ii. Imaging the Renal Arteries and the Aortoiliac Arteries in the Absence of AAA or Aortic Dissection

Effective July 1, 2003, MRA coverage is expanded to include imaging the renal arteries and the aortoiliac arteries in the absence of AAA or aortic dissection. MRA should be obtained in those circumstances in which using MRA is expected to avoid obtaining CA, when physician history, physical examination, and standard assessment tools provide insufficient information for patient management, and obtaining an MRA has a high probability of positively affecting patient management. However, CA may be ordered after obtaining the results of an MRA in those rare instances where medical necessity is demonstrated.

d. Chest

i. Diagnosis of Pulmonary Embolism

Current scientific data has shown that diagnostic pulmonary MRAs are improving due to recent developments such as faster imaging capabilities and gadolinium-enhancement. However, these advances in MRA are not significant enough to warrant replacement of pulmonary angiography in the diagnosis of pulmonary embolism for patients who have no contraindication to receiving intravenous iodinated contrast material. Patients who are allergic to iodinated contrast material face a high risk of developing complications if they undergo pulmonary angiography or computed tomography angiography. Therefore, Medicare will cover MRA of the chest for diagnosing a suspected pulmonary embolism when it is contraindicated for the patient to receive intravascular iodinated contrast material.

ii. Evaluation of Thoracic Aortic Dissection and Aneurysm

Studies have shown that MRA of the chest has a high level of diagnostic accuracy for pre-operative and post-operative evaluation of aortic dissection of aneurysm. Depending on the clinical presentation, MRA may be used as an alternative to other non-invasive imaging technologies, such as transesophageal echocardiography and CT. Generally, Medicare will provide coverage only for MRA or for CA when used as a diagnostic test. However, if both MRA and CA of the chest are used, the physician must demonstrate the medical need for performing these tests.

While the intent of this policy is to provide reimbursement for either MRA or CA, CMS is also allowing flexibility for physicians to make appropriate decisions concerning the use of these tests based on the needs of individual patients. CMS anticipates, however, low utilization of the combined use of MRA and CA. As a result, CMS encourages contractors to monitor the use of these tests and, where indicated, requires evidence of the need to perform both MRA and CA.

C. Contraindications and Nationally Non-Covered Indications

1. Contraindications

MRI is not covered when the following patient-specific contraindications are present:

- It is not covered for patients with cardiac pacemakers or with metallic clips on vascular aneurysms.
- MRI during a viable pregnancy is also contraindicated at this time.
- The danger inherent in bringing ferromagnetic materials within range of MRI units generally constrains the use of MRI on acutely ill patients requiring life support systems and monitoring devices that employ ferromagnetic materials.
- In addition, the long imaging time and the enclosed position of the patient may result in claustrophobia, making patients who have a history of claustrophobia unsuitable candidates for MRI procedures.

2. Nationally Non-Covered Indications

The Centers for Medicare & Medicaid Services (CMS) has determined that MRI of cortical bone and calcifications, and procedures involving spatial resolution of bone and calcifications, are not considered reasonable and necessary indications within the meaning of section 1862(a)(1)(A) of the Social Security Act, and are therefore non-covered.

D. Other

Effective June 3, 2010, all other uses of MRI or MRA for which CMS has not specifically indicated coverage or non-coverage continue to be eligible for coverage through individual local contractor discretion.

(This NCD last reviewed June 2010.)

220.3 - Magnetic Resonance Angiography (MRA) (Effective June 3, 2010) (Replaced with section 220.2)

Back to Top

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Back to Top